

ABSTRACT OF THE DISCLOSURE

The present invention provides a method for identifying a thermostable polymerase having altered fidelity. The method consists of generating a random population of polymerase mutants by mutating at least one amino acid residue of a thermostable polymerase and screening the population for one or more active polymerase mutants by genetic selection. For example, the invention provides a method for identifying a thermostable polymerase having altered fidelity by mutating at least one amino acid residue in an active site O-helix of a thermostable polymerase. The invention also provides thermostable polymerases and nucleic acids encoding thermostable polymerases having altered fidelity, for example, high fidelity polymerases and low fidelity polymerases. The invention additionally provides a method for identifying one or more mutations in a gene by amplifying the gene with a high fidelity polymerase. The invention further provides a method for accurately copying repetitive nucleotide sequences using a high fidelity polymerase mutant. The invention also provides a method for diagnosing a genetic disease using a high fidelity polymerase mutant. The invention further provides a method for randomly mutagenizing a gene by amplifying the gene using a low fidelity polymerase mutant.